IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

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| EXELIXIS, INC., | ) | |
| | ) | |
| Plaintiff, | ) | |
| | ) | |
| v. | ) | C.A. No. 22-228 (RGA) |
| | ) | **CONSOLIDATED** |
| MSN LABORATORIES PRIVATE LIMITED and MSN PHARMACEUTICALS, INC., | ) | |
| | ) | |
| Defendants. | ) | |

**EXELIXIS' REPLY POST-TRIAL BRIEF**
**ON INFRINGEMENT OF U.S. PATENT NO. 11,298,349**

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# TABLE OF AUTHORITIES

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**Federal Cases**

## TABLE OF ABBREVIATIONS

| Abbreviation | Description |
|---|---|
| ’439 patent | U.S. Patent No. 11,091,439 (JTX-1) |
| ’440 patent | U.S. Patent No. 11,091,440 (JTX-2) |
| ’015 patent | U.S. Patent No. 11,098,015 (JTX-3) |
| ’349 patent | U.S. Patent No. 11,298,349 (JTX-4) |
| 1-1 impurity | 6,7-dimethoxy-quinoline-4-ol |
| ANDA | Abbreviated New Drug Application |
| API | Active Pharmaceutical Ingredient |
| Asserted Claims | For the ’349 patent, claim 3<br>For the ’439 patent, claim 4<br>For the ’440 patent, claim 3<br>For the ’015 patent, claim 2 |
| DFOF | MSN’s Rebuttal Proposed Findings of Fact on MSN’s Infringement, D.I. 174 |
| Exelixis | Exelixis, Inc. |
| Exelixis Op. Br. | Exelixis’ Opening Brief on MSN’s Infringement, D.I. 167 |
| FDA | United States Food and Drug Administration |
| FOF | Exelixis’ Proposed Findings of Fact on MSN’s Infringement, D.I. 168 |
| GRASTAR | Granulated corn starch |
| MSN | MSN Laboratories Private Limited and MSN Pharmaceuticals, Inc. |
| MSN’s ANDA | MSN ANDA No. 213878 |
| MSN Resp. Br. | MSN’s Responsive Brief, D.I. 173 |
| NDA | New Drug Application |
| POSA | Person of ordinary skill in the art |

| | |
|---|---|
| Tr. | Final Trial Transcripts |
| UF | Uncontested Facts (D.I. 154, Ex. 1) |
| Zydus | Zydus Worldwide DMCC |

## I. INTRODUCTION

The evidence of infringement is clear. The parties agree that a "glidant" is an excipient that improves the flow properties of a drug mixture. FOF ¶ 19; Exelixis Op. Br. at 5-6; MSN Resp. Br. at 15. The parties also agree that cabozantinib (L)-malate is poorly flowing, and that MSN adds granulated corn starch (GRASTAR) to its ANDA Products in a manner consistent with the use of a glidant. FOF ¶ 23; *see also* MSN Resp. Br. at 5. And there is no dispute that MSN told FDA that granulated cornstarch "enhances the flowability of the granules" and "plays an important role in flow characteristics." FOF ¶¶ 36, 39; DTX-215 at 36, 58.

Faced with this undisputed evidence, MSN resorts to arguments lacking any basis in fact or law. For example, MSN attempts to dismiss its statements to FDA about granulated corn starch as mere summaries of the literature having nothing to do with its ANDA Products. MSN Resp. Br. at 20. MSN also argues that an MSN laboratory notebook, as revised in a demonstrative at trial, is the "only empirical data" on infringement. *Id.* at 8-11. These arguments are meritless and do not undermine the persuasive evidence demonstrating that the GRASTAR in MSN's ANDA Products improves flow and is, therefore, a glidant.

## II. ARGUMENT

### A. MSN's Statements to the FDA Pertain to Its ANDA Products

MSN repeatedly told FDA that granulated corn starch improved flow, which is precisely what glidants do. MSN's clear and admittedly truthful statements to FDA provide strong proof of infringement.[1]

***First***, in its "Justification for the Initial Risk Assessment," MSN told FDA that granulated corn starch "***enhances the flowability*** of the granules." DTX-215 at 36 (emphasis added); FOF

[1] Although MSN attempts to distinguish Exelixis' case law, it admits that courts have credited statements made in a generic defendant's ANDA to find infringement. MSN Resp. Br. at 21-22.

¶ 36. Contrary to MSN's argument (MSN Resp. Br. at 20), there is no reference to scientific literature in MSN's statement. Moreover, the use of the present tense, reference to "minimal concentration," and the article "the" before granules indicate that the statement is not intended to be general and instead specifically refers to the granules in MSN's products. DTX-215 at 36; FOF ¶ 36. This is consistent with Dr. Koleng's testimony that the Initial Risk Assessment is typically generated ***after*** a core formulation for an ANDA product has been identified. FOF ¶ 36. And, even if one were to accept MSN's argument that it was just summarizing the literature for FDA, the alleged summary undermines MSN's position that the literature does not describe granulated corn starch as a glidant. MSN Resp. Br. at 13 n.3. MSN cannot have it both ways.

***Second***, MSN made a similar statement in the portion of its Product Development Report describing the company's studies with GRASTAR. MSN said "[t]he level of Granulated corn Starch ***plays an important role in flow*** characteristics." DTX-215 at 58 (emphasis added); FOF ¶ 39. Although MSN's head of formulations R&D tried to dismiss this statement as summarizing the literature, he admitted (when confronted with the context) that the statements were not based on literature but instead reflected ***MSN's*** studies of GRASTAR during the development of its ANDA Products. Tr. 63:13-15, 64:6-19 (Nithiyanandam); FOF ¶¶ 39, 22; Tr. 144:2-16 (Koleng).

***Third***, although MSN argues that GRASTAR was added to its products to improve dissolution, not flow (MSN Resp. Br. at 6-8), the Product Development Report does not say this. The portion of the Report describing MSN's studies states that GRASTAR ***does*** play an important role in flow but ***did not*** impact dissolution at any of the amounts tested and presented in MSN's ANDA. *See* DTX-215 at 58, 60; FOF ¶ 46. Indeed, MSN ***never*** told FDA that GRASTAR was used to improve the dissolution of its products. *See* DTX-215 at 58-60. MSN's argument that its studies on GRASTAR pertained only to dissolution cannot be reconciled with what it told FDA.

Finally, MSN's focus on the absence of the word "glidant" in its FDA submissions (MSN Resp. Br. at 21) misses the mark. Statements that GRASTAR improved flow, as a glidant does, are sufficient. MSN should be bound by what it told FDA. *Intendis GMBH v. Glenmark Pharms. Inc.*, 822 F.3d 1355, 1362 (Fed. Cir. 2016).

### B. Undisputed Facts Regarding MSN's Manufacturing Process Provide Yet More Evidence that GRASTAR Is a Glidant

MSN does not deny that GRASTAR is added to its ANDA Products at a stage and concentration typical of a glidant (*see* FOF ¶¶ 28-29, 33-35), but argues that these facts do not prove infringement because diluents may also be used in this manner. MSN Resp. Br. at 14-15. MSN's argument fails for at least three reasons. ***First***, MSN's use of GRASTAR in its ANDA Products is consistent with what MSN told FDA about GRASTAR, i.e., that it played an "important role in flow characteristics." *See supra* § II.A. ***Second***, as Exelixis' expert Dr. Koleng testified, GRASTAR is used in such a minimal concentration in MSN's products that it would not have a meaningful impact as a diluent. Tr. 91:1-8 (Koleng); FOF ¶ 44. ***Third***, as the parties agree, excipients can perform multiple functions. FOF ¶ 45; *see, e.g.*, Tr. 247:12-22 (Donovan). Thus, GRASTAR could be ***both*** a glidant and a diluent. Tr. 93:2-6, 90:15-25 (Koleng). In short, the undisputed evidence regarding MSN's use of GRASTAR in its ANDA Products further demonstrates infringement.[2]

### C. MSN's Demonstrative Is Not Evidence

To support its argument that GRASTAR does not improve flow, MSN relies upon a trial demonstrative including an altered version of an entry in an MSN laboratory notebook. MSN Resp. Br. at 10; *compare* DDX-2 (Koleng) at 4, *with* DTX-196 at 86. MSN's characterization of

[2] MSN argues that the use of wet granulation "fully resolved any issue with the API's poor flow." MSN Resp. Br. at 5. Although wet granulation may have improved flow, that does not undermine MSN's unequivocal statements that GRASTAR did too. *See supra* § II.A.

this as "empirical data" on infringement (MSN Resp. Br. at 8-11) is wrong.

First, MSN's trial demonstrative is not evidence. *See IPPV Enters., LLC v. Echostar Commc'ns Corp.*, 191 F. Supp. 2d 530, 565 (D. Del. 2002). As explained in Exelixis' opening brief and by Dr. Koleng at trial, the actual notebook contains an error, but its nature is unclear; the error could be in either the recorded bulk and tap density data or in the calculated outputs, i.e., the Carr Index and Hausner ratios. *See* FOF ¶¶ 55-58; Exelixis' Op. Br. at 10 n.1. MSN's assertion that "the error's origin *was* identified" (MSN Resp. Br. at 10) is not supported by any evidence. Also unsupported is MSN's reliance on its own demonstrative recalculating the Carr Index and Hausner ratios based on an assumption that the bulk and tap density data in the notebook are correct. MSN Resp. Br. at 10 (citing DDX-2 (Koleng) at 4). MSN presented no testimony or evidence substantiating this assumption. The only witness asked about MSN's demonstrative—Dr. Koleng—did not dispute MSN's numerical calculations, but clearly stated that he could not rely on the notebook given the unexplained discrepancy.[3] Tr. 180:16-182:11, 107:1-19 (Koleng).

Second, the study in the notebook compared formulations with GRASTAR versus unmodified corn starch, a well-known glidant; it did not compare formulations with and without a glidant. *See* DTX-196 at 46-48, 84-86; Tr. 1046:3-17. Thus, even if the information in the notebook could be relied upon (which it cannot), the data does not show that GRASTAR failed to improve flow. FOF ¶ 59.

Finally, contrary to MSN's assertion (MSN Resp. Br. at 8-11), the lab notebook underlying the demonstrative is not the "only empirical data" reflecting GRASTAR's properties as a glidant. Other "empirical data"—verifiable by observation or experience, rather than theory or

[3] As Dr. Koleng explained at trial, his opinion does not rely on the lab notebook and is supported by other evidence. Tr. 107:1-24 (Koleng).

pure logic—was adduced at trial, including that: (1) the cabozantinib (L)-malate API flows poorly and required improvement (DTX-215 at 34; FOF ¶ 23); (2) the precise concentration (9.71%) at which GRASTAR is added is indicative of a glidant (FOF ¶¶ 28, 44); and (3) the stage of manufacturing at which GRASTAR is incorporated (i.e., after granulation, pre-lubrication) is typical for a glidant (FOF ¶¶ 33-35). Moreover, MSN's statements to FDA are admissions to a regulatory body that bear directly on the question of infringement. *Intendis*, 822 F.3d at 1362.

In short, MSN's trial demonstrative does not constitute "empirical data" at all, let alone disprove MSN's statements to FDA that GRASTAR plays an important role in flow.

**D. Several MSN Arguments Are Not Relevant to Infringement**

Several of MSN's arguments are not relevant to the infringement analysis. ***First***, MSN's focus on its alleged ***intention*** to use GRASTAR as a diluent (MSN Resp. Br. at 1, 5-6, 8) is misplaced. A direct infringer's intent is immaterial to infringement. *See Hilton Davis Chem. Co. v. Warner-Jenkinson Co.*, 62 F.3d 1512, 1527 (Fed. Cir. 1995) (en banc) ("[I]ntent is not an element of direct infringement, whether literal or by equivalents.… Infringement is, and should remain, a strict liability offense."), *rev'd on other grounds*, 520 U.S. 17, 35 (1997); *First Years, Inc. v. Munchkin, Inc.*, 575 F. Supp. 2d 1002, 1021 (W.D. Wis. 2008) ("Whether the holes [in the accused product] meet the claim requirements as a result of unintentional manufacturing error or intentional product design is irrelevant; intent is not an element of direct infringement.").[4]

***Second***, contrary to MSN's insinuation (MSN Resp. Br. at 5, 8), testing is not required to prove infringement. *See, e.g.*, *C.R. Bard Inc. v. AngioDynamics, Inc.*, 979 F.3d 1372, 1379 (Fed. Cir. 2020) (direct testing not required where circumstantial evidence supports infringement). This

[4] Although not relevant to direct infringement, intent is an element of inducement. As set forth in Exelixis' opening brief, MSN separately possesses the requisite intent for inducement. FOF ¶¶ 60-61; Exelixis' Op. Br. at 14-15.

is especially true where MSN has made "representation[s] to a federal regulatory body that [are] directly on point" to infringement. *Intendis*, 822 F.3d at 1362.

***Third***, as even MSN's expert admits, the term "glidant" in the '349 patent does not require any particular mechanism, nor do any references on which MSN relies. *See* Tr. 230:16-19, 230:25-232:23 (Donovan); FOF ¶ 21. Even if it did, Exelixis presented evidence that GRASTAR improves flow through at least one of these "mechanisms." FOF ¶¶ 47-54.

## III. CONCLUSION AND REMEDIES

For the reasons above, Exelixis respectfully requests that the Court find claim 3 of the '349 patent infringed and order all remedies specified in Exelixis' opening brief.

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February 20, 2024

**CERTIFICATE OF SERVICE**

I hereby certify that on February 20, 2024, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on February 20, 2024, upon the following in the manner indicated:

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